Meta-analysis of randomized trials on the efficacy of posterior pericardiotomy in preventing atrial fibrillation after coronary artery bypass surgery

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Objective: Posterior pericardiotomy is considered a method to reduce the incidence of atrial fibrillation after cardiac surgery. Its efficacy in preventing atrial fibrillation and supraventricular arrhythmias after coronary artery bypass surgery has been evaluated in the present meta-analysis.

Methods: This meta-analysis was performed in accordance with the *Cochrane Handbook for Systematic Reviews*.

Results: The search yielded 6 prospective, randomized studies reporting on postoperative atrial fibrillation in 763 patients after coronary artery bypass grafting. The cumulative incidence of atrial fibrillation was 10.8% in the posterior pericardiotomy group (PP group) and 28.1% in the control group (I^2 68%, random effect: $P = .003$; odds ratio [OR], 0.33; 95% confidence interval [CI], 0.16–0.69). Supraventricular arrhythmias occurred in 13.8% of patients in the PP group and 35.4% in the control group (I^2 70%, random effect: $P = .002$; OR, 0.31; 95% CI, 0.15–0.65). Early pericardial effusion (6.9% vs 46.2%; I^2 67%; random effect: $P < .0001$; OR, 0.10; 95% CI, 0.04–0.28) and late pericardial effusion (0% vs 11.3%; I^2 0%; fixed effect: $P = .0001$; OR, 0.04; 95% CI, 0.01–0.21) were significantly less frequent in the PP group. Pleural effusion (5 studies included: 22.2% vs 17.1%; I^2 0%; fixed effect: $P = .10$; OR, 1.40; 95% CI, 0.94–2.08) and pulmonary complications were only slightly more frequent in the PP group (4 studies included: 3.6% vs 2.5%; I^2 0%; fixed effect: $P = .46$; OR, 1.45; 95% CI, 0.54–3.86).

Conclusions: Posterior pericardiotomy seems to significantly reduce the incidence of postoperative atrial fibrillation and supraventricular arrhythmias after coronary artery bypass grafting. The marked reduction of postoperative pericardial effusion after posterior pericardiotomy suggests that pericardial effusion is one of the main triggers involved in the development of atrial fibrillation after cardiac surgery. (J Thorac Cardiovasc Surg 2010;139:1158-61)

Atrial fibrillation (AF) is the most common complication occurring after cardiac surgery and is associated with hemodynamic instability, prolonged hospital stay, stroke, and increased costs.[1,2] AF is also one of the main causes of hospital readmission.[3] Pathogenesis of AF after cardiac surgery is multifactorial, and mechanisms are still largely unknown. Increase in circulating catecholamines, heightened sympathetic and parasympathetic tone, atrial stretch, transcellular fluid and electrolyte shifts, metabolic abnormalities, inflammation, and pericarditis are believed to be the most important factors contributing to AF after cardiac surgery.[4]

A significant number of trials have been performed showing the efficacy of several drugs in preventing postoperative AF in these patients.[1,5] However, the use of these drugs for risk reduction of AF is not free of complications and is associated with marked incremental costs.

Posterior pericardiotomy (PP) is considered a method to reduce the risk of AF inasmuch as it allows drainage of pericardial blood/effusion into the left pleural space, reducing the incidence of pericardial effusion, which may trigger AF.[6] The present meta-analysis was carried out to evaluate the efficacy of this method in preventing postoperative AF and other supraventricular arrhythmias, as well as pericardial effusion.

MATERIAL AND METHODS

This meta-analysis of randomized trials was performed in accordance with the *Cochrane Handbook for Systematic Reviews*.[7] Reference search was performed through PubMed and Cochrane Library up to February 2009 for trials evaluating the efficacy of PP in preventing AF after cardiac surgery. The following words were used in the search: posterior pericardiotomy, pericardial fenestration, and pericardial window. Handbooks as well as cardiology and cardiac surgery journals have been searched as well.

Only prospective, randomized studies with allocation to PP or control in adult patients undergoing any type of cardiac surgery and reporting at least on postoperative AF were included in the present analysis. Clinical variables and outcome end points were reported as originally defined by the authors.

The primary outcome end points of this study are AF and supraventricular arrhythmias. Secondary outcome end points are pericardial effusion, pleural effusion, and pulmonary complications.

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Abbreviations and Acronyms

AF = atrial fibrillation
CABG = coronary artery bypass grafting
CI = confidence interval
OR = odds ratio
PP = posterior pericardiotomy
RR = risk ratio

Data Collection and Analysis

Both authors independently abstracted data from all eligible studies using a standardized Excel file. We retrieved data on study design, study size, patient demographics, type of surgery, intraoperative data, and any outcome end points.

The risk of bias has been assessed independently by both of us according to the Cochrane Collaboration criteria for assessing risk of bias.[7] Disagreement has been resolved by consensus. Trials that met eligibility criteria have been assessed for generation of random allocation sequence, allocation concealment, blinding of intervention, incomplete outcome data, freedom of selective reporting, and freedom from other biases. Missing data have been evaluated and a dropout rate of less than 5% has been considered as acceptable.

Meta-analysis was performed using Review Manager 5.0.18 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008). Outcome end points were expressed as odds ratio (OR) and risk ratio (RR) with 95% confidence interval (CI). Continuous variables were reported as weighted mean differences and 95% CI. Heterogeneity has been assessed by using I^2 and χ^2 test. I^2 less than 40% has been considered as nonimportant heterogeneity. In case of important heterogeneity, we have used the random-effects model. The small number of studies included in this meta-analysis, as well as the paucity of clinical and operative variables reported in the studies, prevented meta-regression analysis.

RESULTS

The search yielded 9 articles that were pertinent with this issue. Two of them were excluded because they were case reports. Another article, a prospective randomized study on the efficacy of PP in heart valve surgery, was excluded because no data on the incidence of postoperative AF were reported.[8] Data on postoperative AF that occurred in the third trial were requested from the authors, but they were not able to provide any information on this outcome end point. Thus, 6 prospective, randomized studies reporting on postoperative AF after conventional coronary artery bypass surgery (CABG) have been included in the present meta-analysis.[6,9-13]

In all, 763 patients were evaluated in these 6 studies, 389 patients in the PP groups and 374 in the control groups. PP was performed in all studies as a longitudinal incision parallel and posterior to the phrenic nerve, extending from the left inferior pulmonary vein to the diaphragm according to the technique described by Mulay and colleagues.[6] One drain was inserted into the left pleural cavity and another into the anterior mediastinum.

Patients were monitored for arrhythmias during the in-hospital stay. Continuous electrocardiographic monitoring was performed during the first 48 to 96 postoperative hours and then daily or as required.[6,9-13]

Regarding the methodologic quality of the studies, only 2 of them reported on adequate sequence generation, all studies were free of selective reporting and other biases, and information about allocation concealment, blinding, and incomplete outcome data were not reported in any of them.

No difference in terms of patients' ages (I^2 56%; random effect: $P = .70$; mean difference –0.30; 95% CI, –1.36 to 0.77), aortic crossclamping time (I^2 80%; random effect: $P = .71$; mean difference –0.84; 95% CI, –5.22 to 3.55), and cardiopulmonary bypass duration (I^2 51%; random effect: $P = .30$; mean difference –1.36; 95% CI, –3.91 to 1.19) were observed between the study groups (Table 1). Drainage blood loss was somewhat lower in the control group (I^2 87%; random effect: $P = .41$; mean difference 24.38; 95% CI, –33.89 to 82.64), but the difference was not statistically significant.

Not enough data were available for analysis of postoperative mortality and reoperation.

The cumulative incidence of AF was 10.8% in the PP group and 28.1% in the control group (I^2 68%; random effect: $P = .003$; OR, 0.33; 95% CI, 0.16–0.69; RR, 0.41; 95% CI, 0.22–0.76) (Figure 1, *A*).

The cumulative incidence of supraventricular arrhythmias was 13.8% in the PP group and 35.4% in the control group (I^2 70%; random effect: $P = .002$; OR, 0.31; 95% CI, 0.15–0.65; RR, 0.41; 95% CI, 0.23–0.74) (Figure 1, *B*).

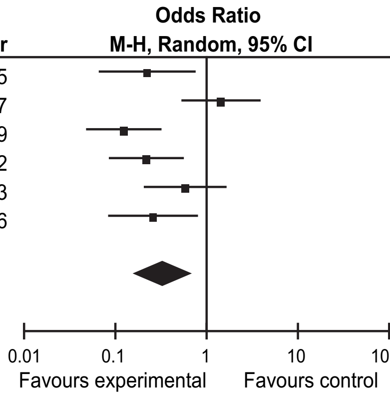
TABLE 1. Summary of studies included in the meta-analysis

		No. of patients		Patients' age (y)		Aortic crossclamping time (min)		CPB duration (min)	
Authors	Type of surgery	Control	PP	Control	PP	Control	PP	Control	PP
Mulay et al[6]	CABG	50	50	60.1 ± 3.2	59.1 ± 8.9	43 ± 6	46 ± 20	85 ± 4	90 ± 33
Asimakopoulos et al[9]	CABG	50	50	60.1 ± 9.0	62.3 ± 8.2	33 ± 8	35 ± 2	62 ± 17	66 ± 17
Kuralay et al[10]	CABG	100	100	62.8 ± 5.4	64.2 ± 8.9	43 ± 9	36 ± 12	51 ± 4	48 ± 5
Farsak et al[11]	CABG	75	75	61 ± 8	57 ± 12	40 ± 9	35 ± 11	61 ± 9	57 ± 6
Arbatli et al[12]	CABG	59	54	61 ± 2	61 ± 9	60 ± 19	58 ± 17	112 ± 35	117 ± 32
Ekim et al[13]	CABG	50	50	62.5 ± 4.9	62 ± 7	62 ± 12	63 ± 19	87 ± 26	89 ± 21

CPB, Cardiopulmonary bypass; *PP*, posterior pericardiotomy; *CABG*, coronary artery bypass grafting. Continuous variables are reported as the mean ± standard deviation.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Mulay 1995	4	50	14	50	14.9%	0.22 [0.07, 0.74]	1995
Asimakopoulos 1997	12	50	9	50	17.2%	1.44 [0.55, 3.80]	1997
Kuralay 1999	6	100	34	100	17.7%	0.12 [0.05, 0.31]	1999
Farsak 2002	7	75	24	75	17.8%	0.22 [0.09, 0.55]	2002
Arbatli 2003	7	54	12	59	16.7%	0.58 [0.21, 1.61]	2003
Ekim 2006	5	50	15	50	15.8%	0.26 [0.09, 0.78]	2006
Total (95% CI)		**379**		**384**	**100.0%**	**0.33 [0.16, 0.69]**	
Total events	41		108				

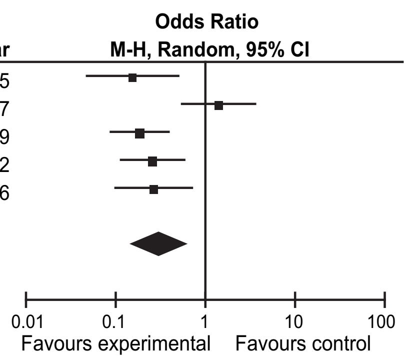
Heterogeneity: Tau² = 0.57; Chi² = 15.78, df = 5 (P = 0.008); I² = 68%
Test for overall effect: Z = 2.94 (P = 0.003)



A

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Mulay 1995	4	50	18	50	16.9%	0.15 [0.05, 0.50]	1995
Asimakopoulos 1997	13	50	10	50	19.9%	1.41 [0.55, 3.59]	1997
Kuralay 1999	11	100	40	100	22.5%	0.19 [0.09, 0.39]	1999
Farsak 2002	10	75	28	75	21.5%	0.26 [0.11, 0.58]	2002
Ekim 2006	7	50	19	50	19.3%	0.27 [0.10, 0.71]	2006
Total (95% CI)		**325**		**325**	**100.0%**	**0.31 [0.15, 0.65]**	
Total events	45		115				

Heterogeneity: Tau² = 0.51; Chi² = 13.44, df = 4 (P = 0.009); I² = 70%
Test for overall effect: Z = 3.07 (P = 0.002)



B

FIGURE 1. Forest plots of comparison between posterior pericardiotomy (experimental) group and control group for prevention of postoperative (A) atrial fibrillation and (B) supraventricular arrhythmias after coronary artery bypass surgery. *CI,* Confidence interval; *M-H,* Mantzel-Haenzel method.

Early pericardial effusion (4 studies included: 6.9% vs 46.2%; I^2 67%; random effect: $P < .0001$; OR, 0.10; 95% CI, 0.04–0.28; RR, 0.17; 95% CI, 0.07–0.42) as well as late pericardial effusion (4 studies included: 0% vs 11.3%; I^2 0%; fixed effect: $P = .0001$; OR, 0.04; 95% CI, 0.01–0.21; RR, 0.05; 95% CI, 0.01–0.24) were significantly less frequent in the PP group.

Pleural effusion (5 studies included: 22.2% vs 17.1%; I^2 0%; fixed effect: $P = .10$; OR, 1.40; 95% CI, 0.94–2.08; RR, 1.29; 95% CI, 0.95–1.74) and pulmonary complications were only slightly more frequent in the PP group (4 studies included: 3.6% vs 2.5%; I^2 0%; fixed effect: $P = .46$; OR, 1.45; 95% CI, 0.54–3.86; RR, 1.43; 95% CI, 0.55–3.69).

DISCUSSION

The results of this meta-analysis indicate that PP markedly reduces the incidence of AF and supraventricular arrhythmias after CABG. The OR of PP (OR, 0.31) in preventing postoperative AF is even better than that with the use of beta-blockers, sotalol, corticosteroids, and amiodarone as estimated in previous meta-analyses (OR ranging from 0.36 to 0.48).[1,5]

The antiarrhythmic effect of PP was associated with a significant reduction in the incidence of early and late pericardial effusion. It is likely that the reduced risk of AF after PP is due to decreased pericardial effusion, which may trigger postoperative supraventricular arrhythmias. The mechanisms by which pericardial effusion may lead to these arrhythmias are not clear. We can just speculate that a certain amount of fluid/hematoma into the pericardium may represent a mechanical stimulus to the atria, whose function can be affected by external compression.

The slightly increased blood loss in the PP group suggests that this method provides an effective pathway of drainage to the pleural cavity of pericardial blood/effusion, which otherwise would have been collected in the pericardium and compressed the heart. Importantly, pleural effusion and pulmonary complications were not significantly more frequent in the PP group.

These results are not conclusive inasmuch as further studies with better methodology are needed. In fact, the methodogic quality of the included studies is far from being optimal. The method of randomization was reported in only 2 studies and information regarding allocation concealment, blinding, and incomplete outcome data were not reported. Importantly, there are no data regarding the use of drugs for AF prophylaxis, which represents a major bias for correct interpretation of these data. Other major pitfalls are the lack of data on postoperative hemodynamic instability, reoperation for bleeding/pericardial effusion, and potential AF-related complications such as stroke, renal failure, prolonged length of in-hospital stay, and readmission.

PP is easy to do and it is cost-free. However, it is not free of complications. Besides the potential risk of cardiac herniation, bypass grafts after CABG can protrude through and be squeezed by the edges of the PP.[14] These complications are likely to be minimized by performing a limited PP at the end of the procedure at a distance from the bypass grafts. However, the risk of such PP-related complications also deserves further evaluation.

In conclusion, this meta-analysis suggests that adding PP during CABG seems to reduce the incidence of postoperative AF and supraventricular arrhythmias. The marked reduction of postoperative pericardial effusion observed after PP suggests that the former is one of the main triggers of AF occurring after cardiac surgery.

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